



Complete Summary

GUIDELINE TITLE

Iron ingestion: an evidence-based consensus guideline for out-of-hospital management.

BIBLIOGRAPHIC SOURCE(S)

Manoguerra AS, Erdman AR, Booze LL, Christianson G, Wax PM, Scharman EJ, Woolf AD, Chyka PA, Keyes DC, Olson KR, Caravati EM, Troutman WG. Iron ingestion: an evidence-based consensus guideline for out-of-hospital management. Clin Toxicol (Phila) 2005; 43(6):553-70. [PubMed](#)

GUIDELINE STATUS

This is the current release of the guideline.

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SCOPE

DISEASE/CONDITION(S)

Iron poisoning

Note:

- This guideline applies to ingestion of iron alone. Co-ingestion of additional substances could require different referral and management recommendation depending on the combined toxicities of the substances.
- The guideline considers acute exposure to iron only, which is defined as a single exposure or multiple exposures occurring within a period of 8 hours. The guideline does not deal with chronic oral exposures or parenteral iron exposures.

GUIDELINE CATEGORY

Evaluation
Management
Risk Assessment

CLINICAL SPECIALTY

Emergency Medicine
Family Practice
Internal Medicine
Pediatrics

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Emergency Medical Technicians/Paramedics
Nurses
Pharmacists
Physicians

GUIDELINE OBJECTIVE(S)

To assist U.S. poison center personnel in the appropriate out-of-hospital triage and initial management of patients with suspected ingestions of iron by

- Describing the manner in which an ingestion of iron might be managed
- Identifying the key decision elements in managing cases of iron ingestion
- Providing clear and practical recommendations that reflect the current state of knowledge
- Identifying needs for research

TARGET POPULATION

- Children less than 6 years of age with acute iron exposure
- Patients 6 years of age or older with acute iron exposure
- Pregnant women with acute iron exposure

INTERVENTIONS AND PRACTICES CONSIDERED

Evaluation

1. Assessment of key decision points for triage:
 - Patient intent
 - Time of the ingestion
 - Symptoms or underlying medical conditions
 - Estimated dose and formulation of iron ingested and other co-ingestants

Management

1. Referral to an acute care medical facility (emergency department)
2. Home observation
3. Note: the following medications for gastrointestinal decontamination were considered but not recommended for out-of-patient management: ipecac syrup, activated charcoal, cathartics, and oral complexing agents, such as bicarbonate or phosphate solutions
4. Follow-up

MAJOR OUTCOMES CONSIDERED

- Threshold dose of iron for the development of toxicity
- Dose requiring referral to a healthcare facility

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
 Hand-searches of Published Literature (Secondary Sources)
 Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Literature Search

The National Library of Medicine's PubMed database was searched (through November 2003) using iron (poisoning) or iron (toxicity) or ferrous compounds (poisoning) or ferrous compounds (toxicity) as Medical Subject Heading (MeSH) terms, all limited to humans. The PubMed database was searched again (through November 2003) using iron or ferrous as textwords (title, abstract, MeSH term, CAS number) plus either poison* or overdos* or tox* or intox*, limited to humans. This same process was repeated in International Pharmaceutical Abstracts (1970 to November 2003, excluding abstracts of meeting presentations), Science Citation Index (1977 to November 2003), Database of Abstracts of Reviews of Effects (accessed November 2003), Cochrane Database of Systematic Reviews (accessed November 2003), and Cochrane Central Register of Controlled Trials (accessed November 2003). Reactions (1980 to November 2003), the iron poisoning management in POISINDEX, and the bibliographies of recovered articles were reviewed to identify previously undiscovered articles. Furthermore, North American Congress of Clinical Toxicology abstracts published in the Journal of Toxicology-Clinical Toxicology (1995–2003) were reviewed for original human data. The iron chapter bibliographies in four major toxicology textbooks were reviewed for citations of additional articles with original human data. Finally, The Toxic Exposure Surveillance System (TESS) maintained by the American Association of Poison Control Centers was searched for deaths resulting from iron poisoning. These cases were abstracted for use by the panel.

Article Selection

The recovered citations were entered into an EndNote library and duplicate entries were eliminated. The abstracts of the remaining articles were reviewed, looking

specifically for those that dealt with estimations of mg/kg or ingested doses with or without subsequent signs or symptoms, time of onset of symptoms, and management techniques that might be suitable for out-of-hospital use (e.g., gastrointestinal decontamination). Articles excluded were those that did not meet either of the preceding criteria, did not add new data (e.g., some reviews, editorials), or that exclusively described inpatient only procedures (e.g., whole bowel irrigation). Specific animal studies were included only if they were relevant to panel recommendations.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Articles were assigned level-of-evidence scores based on the Grades of Recommendation table developed by the Centre for Evidence-Based Medicine at Oxford University. Single case reports were classified along with case series as level 4.

Levels of Evidence	Description of Study Design
1a	Systematic review (with homogeneity) of randomized clinical trials
1b	Individual randomized clinical trials (with narrow confidence interval)
1c	All or none (all patients died before the drug became available, but some now survive on it; or when some patients died before the drug became available, but none now die on it)
2a	Systematic review (with homogeneity) of cohort studies
2b	Individual cohort study (including low quality randomized clinical trial)
2c	"Outcomes" research
3a	Systemic review (with homogeneity) of case-control studies
3b	Individual case-control study
4	Case series, single case reports (and poor quality cohort and case control studies)
5	Expert opinion without explicit critical appraisal or based on physiology or bench research
6	Abstracts

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Data Extraction

All articles that were retrieved from the original search were reviewed by a single abstractor. Each article was assigned a level of evidence score from 1 to 6 (see the "Rating Scheme for the Strength of the Evidence" field); the complete paper was reviewed for original human data regarding the toxic effects of iron or original human data directly relevant to the out-of-hospital management of patients with iron overdose. Relevant data (e.g., dose of iron, resultant effects, time of onset of effects, therapeutic interventions or decontamination measures given, efficacy or results of any interventions, and overall patient outcome) were compiled into a table and a brief summary description of each article was written. This full evidence table is available at

<http://www.aapcc.org/DiscGuidelines/IronEvidenceTable.pdf>.

The completed table of all abstracted articles was then forwarded to the panel members for review and consideration in developing the guideline. Every attempt was made to locate significant foreign language articles and have their crucial information extracted, translated, and tabulated. Copies of all of the abstracted articles were made available for reading by the panel members on a secure American Association of Poison Control Centers (AAPCC) Web site.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Delphi)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

An expert consensus panel was established to oversee the guideline development process (see Appendix 1 in the original guideline document). The American Association of Poison Control Centers (AAPCC), the American Academy of Clinical Toxicology (AACT), and the American College of Medical Toxicology (ACMT) appointed members of their organizations to serve as panel members. To serve on the expert consensus panel, an individual had to have an exceptional track record in clinical care and scientific research in toxicology, board certification as a clinical or medical toxicologist, significant U.S. poison center experience, and be an opinion leader with broad esteem. Two Specialists in Poison Information were included as full panel members to provide the viewpoint of the end-users of the guideline.

Guideline Writing and Review

A guideline draft was prepared by the primary author. The draft was submitted to the expert consensus panel for comment. Using a modified Delphi process, comments from the expert consensus panel members were collected, copied into a table of comments, and submitted to the primary author for response. The primary author responded to each comment in the table and, when appropriate, the guideline draft was modified to incorporate changes suggested by the panel. The revised guideline draft was again reviewed by the panel and, if there was no strong objection by any panelist to any of the changes made by the primary author, the draft was prepared for the external review process.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

The rating scheme for the strength of the recommendation (A-D, Z) is directly tied to the level of evidence supporting the recommendation.

Grades of Recommendation	Levels of Evidence
A	1a
	1b
	1c
B	2a
	2b
	2c
	3a
	3b
C	4
D	5
Z	6

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

External review of the second draft was conducted by distributing it electronically to American Association of Poison Control Centers (AAPCC), American Academy of Clinical Toxicology (AACT), and American College of Medical Toxicology (ACMT) members and the secondary review panel. The secondary review panel consisted of representatives from the federal government, public health, emergency services, pediatrics, pharmacy practice, and consumer organizations (see Appendix 3 in the original guideline). Comments were submitted via a discussion thread on the AAPCC Web site or privately through e-mail communication to AAPCC staff. All submitted comments were stripped of any information that would identify their sources, copied into a table of comments, and reviewed by the expert consensus panel and the primary author. The primary author responded to each comment in the table and his responses and subsequent changes in the guideline were reviewed and accepted by the panel. Following a meeting of the expert consensus panel, the final revision of the guideline was prepared.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Grades of recommendation (A-D, Z) and levels of evidence (1a-6) are defined at the end of the "Major Recommendations" field.

1. Patients with stated or suspected self-harm or who are victims of malicious administration of an iron product should be referred to an acute care medical facility immediately. This activity should be guided by local poison center procedures. In general, this should occur regardless of the amount ingested (Grade D).
2. Pediatric or adult patients with a known ingestion of 40 mg/kg or greater of elemental iron in the form of adult ferrous salt formulations or who have severe or persistent symptoms related to iron ingestion should be referred to a healthcare facility for medical evaluation. Patients who have ingested less than 40 mg/kg of elemental iron and who are having mild symptoms can be observed at home. Mild symptoms, such as vomiting and diarrhea, occur frequently. These mild symptoms should not necessarily prompt referral to a healthcare facility. Patients with more serious symptoms, such as persistent vomiting and diarrhea, alterations in level of consciousness, hematemesis, and bloody diarrhea require referral. The same dose threshold should be used for pregnant women; however, when calculating the mg/kg dose ingested, the pre-pregnancy weight of the woman should be used (Grade C).
3. Patients with ingestions of children's chewable vitamins plus iron should be observed at home with appropriate follow-up. The presence of diarrhea should not be the sole indicator for referral as these products are often sweetened with sorbitol. Children may need referral for the management of dehydration if vomiting or diarrhea is severe or prolonged (Grade C).
4. Patients with unintentional ingestions of carbonyl iron or polysaccharide-iron complex formulations should be observed at home with appropriate follow-up (Grade C).
5. Ipecac syrup, activated charcoal, cathartics, or oral complexing agents, such as bicarbonate or phosphate solutions, should not be used in the out-of-hospital management of iron ingestions (Grade C).
6. Asymptomatic patients are unlikely to develop symptoms if the interval between ingestion and the call to the poison center is greater than 6 hours. These patients should not need referral or prolonged observation. Depending on the specific circumstances, follow-up calls might be indicated (Grade C).

Definitions:

Grades of Recommendation and Levels of Evidence

Grades of Recommendation	Levels of Evidence	Description of Study Design
A	1a	Systematic review (with homogeneity) of randomized clinical trials
	1b	Individual randomized clinical trials (with narrow confidence interval)
	1c	All or none (all patients died before the drug became available, but some now survive on it; or when some patients died before the drug became available, but none now die on it.)
B	2a	Systematic review (with homogeneity) of cohort studies
	2b	Individual cohort study (including low quality randomized clinical trial)

Grades of Recommendation	Levels of Evidence	Description of Study Design
	2c	"Outcomes" research
	3a	Systemic review (with homogeneity) of case-control studies
	3b	Individual case-control study
C	4	Case series, single case reports (and poor quality cohort and case control studies)
D	5	Expert opinion without explicit critical appraisal or based on physiology or bench research
Z	6	Abstracts

CLINICAL ALGORITHM(S)

An algorithm is provided in Appendix 4 of the original guideline document for the triage of patients with iron ingestions.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate out-of-hospital triage and initial management of patients with suspected ingestions of iron

POTENTIAL HARMS

Not stated

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- This guideline has been developed for the conditions prevalent in the US. While the toxicity of iron is not expected to vary in a clinically significant manner in other nations, the out-of-hospital conditions could be much different. This guideline should not be extrapolated to other settings unless it has been determined that the conditions assumed in this guideline are present.
- This guideline is based on an assessment of current scientific and clinical information. The expert consensus panel recognizes that specific patient care decisions may be at variance with this guideline and are the prerogative of

the patient and health professionals providing care, considering all of the circumstances involved.

- The toxic dose for various iron products was difficult to evaluate from the literature for several reasons:
 - Histories of ingestion were often reported as unreliable.
 - Many different iron-containing products are or were on the market with varying elemental iron content.
 - Patients or their family members or the authors of the articles often failed to identify the exact product or list its elemental iron content.
 - The bioavailability of iron varies substantially between products.
 - Vomiting and diarrhea often occurred after ingestion and could have resulted in removal of some iron from the gastrointestinal tract.
 - In many patients, treatment procedures performed in a hospital might have influenced the outcome.
 - Many reports did not provide the doses in a per kilogram basis, making comparisons between reported patients difficult.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Clinical Algorithm

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better

IOM DOMAIN

Effectiveness
Timeliness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Manoguerra AS, Erdman AR, Booze LL, Christianson G, Wax PM, Scharman EJ, Woolf AD, Chyka PA, Keyes DC, Olson KR, Caravati EM, Troutman WG. Iron ingestion: an evidence-based consensus guideline for out-of-hospital management. Clin Toxicol (Phila) 2005; 43(6):553-70. [PubMed](#)

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2005 May 3

GUIDELINE DEVELOPER(S)

American Association of Poison Control Centers

SOURCE(S) OF FUNDING

Maternal and Child Health Bureau, Health Resources and Services Administration,
U.S. Department of Health and Human Services

GUIDELINE COMMITTEE

Not stated

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

There are no potential conflicts of interest reported by the expert consensus panel or project staff regarding this guideline.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the [American Association of Poison Control Centers Web site](#).

Print copies: Available from the American Association of Poison Control Centers, 3201 New Mexico Avenue NW, Suite 330, Washington, DC 20016

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on October 27, 2005. The information was verified by the guideline developer on November 28, 2005.

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